

Treximet Executive Summary

This information is provided in response to your request for information about *Treximet*®(sumatriptan and naproxen sodium) Tablets. *Treximet* is a single-tablet formulation of sumatriptan 85 mg, formulated with RT Technology, and naproxen sodium 500 mg.

- Important safety information is found in the attached Prescribing Information.
- The prescribing information for this product contains a boxed warning. Please consult the WARNING section of the attached prescribing information for further details and for important safety information.

MIGRAINE IS A MULTIMECHANISTIC DISEASE

Current understanding of the pathophysiology of migraine suggests that there are multiple mechanisms involved, including neurochemical release, vasodilation, inflammation, and prostaglandin production.^(1,2,3) Individual migraine-specific monotherapies address some, but not all of the multiple components of migraine.

ACUTE MIGRAINE THERAPY: STRATIFIED CARE PROVEN SUPERIOR TO STEP CARE

Available guidelines recommend various treatment options for the treatment of acute migraine. Results of the Disability in Strategies of Care (DISC) Study showed that stratified care provided a significantly greater response and less disability time across 6 attacks compared with step care across attacks and step care within attacks.⁽⁴⁾

OPPORTUNITIES FOR IMPROVEMENT:

Patients are Currently Selecting Step Care Approach to Managing Migraine

Data suggest that patients with access to multiple acute migraine therapies are practicing step care. A survey of 425 migraineurs showed that 71% used multiple medications to treat their migraines.⁽⁵⁾ Over half reported using a step care approach within attack, and 17% used a rescue medication. Similarly, in a managed care population of migraineurs who had previously treated an attack with a triptan plus an NSAID, approximately one quarter chose to treat their next attack with an NSAID first, followed by a triptan later.⁽⁶⁾

Use of Opioids/Narcotics is Prevalent

Data also show that the use of opioids and narcotics is extensive. An analysis of migraineurs in a large managed care database found that 38% of migraine patients compared to 24% for matched controls had filled a narcotic.⁽⁷⁾ Alarming, 7% of migraine cases filled only narcotic medications with no fills for other medications commonly used to treat headache.

Current Therapies Don't Always Work and Result in Redosing or Use of Rescue

Baseline demographics from two studies evaluating patients refractory to short-acting triptans showed that the most common reason for study enrollment was lack of efficacy with prior therapy.^(8,9) ⁽¹⁰⁾

Dissatisfaction with Current Therapy

At screening for a long-term safety study, only about half of patients considered themselves to be satisfied or very satisfied with their previous treatment.⁽¹¹⁾ Not surprisingly, a study by Bigal, et al showed that 80% of patients would be willing to try another acute migraine therapy.⁽¹²⁾

TREXIMET: DISTINCT PHARMACOKINETIC PROFILE

Treximet is a single tablet containing 85 mg sumatriptan, as the succinate salt, formulated with RT Technology™ and 500 mg naproxen sodium. *Treximet* is formulated with a distinct pharmacokinetic profile that aligns with and targets the multiple mechanisms of migraine.⁽¹³⁾ ⁽¹⁴⁾

TREXIMET: EXTENSIVE CLINICAL TRIAL PROGRAM

Over 3,500 patients have treated approximately 30,000 migraine attacks to date with *Treximet*.⁽¹⁵⁾

The clinical program for *Treximet* is comprised of ten randomized, double-blind, placebo-controlled, multicenter studies.^(16,17) ^(8,9,18,19) ^(20,21,22,23,10,24) In addition, a 12-month, open-label, multi-attack, repeat-dose study was completed.⁽²⁵⁾

TREXIMET: SUPERIOR EFFICACY VERSUS SUMATRIPTAN 85 MG

Treximet provided superior results across a variety of efficacy outcomes versus sumatriptan 85 mg in two randomized, double-blind trials in patients treating moderate-to-severe migraine pain.^(16,17,26)

TREXIMET: EFFICACY AT EARLY TIMEPOINTS

Treximet provided superior pain relief and pain free results at 2 and 4 hours across multiple studies evaluating treatment of moderate-to-severe migraine pain or mild migraine pain.^(16,17) ^(8,9,18,19,20,21,10,24) *Treximet* also provided superior migraine free results, one of the most difficult outcomes to achieve, at 2 and 4 hours across multiple studies.

TREXIMET: SUSTAINED EFFICACY

Treximet provided superior sustained pain relief (2-24 hours) versus sumatriptan 85 mg, naproxen sodium 500 mg, and placebo in pivotal efficacy trials of moderate-severe migraine pain.^(16,17) *Treximet* also provided superior sustained pain-free results (2-24 hours) across multiple studies evaluating treatment of moderate-to-severe migraine pain or mild pain.^(16,17) ^(8,9,18,19,20,21,22,23,10,24) In addition, in all of these studies, the use of rescue medication was significantly reduced in patients taking *Treximet*.

TREXIMET: CONSISTENCY OF RESPONSE

In two studies evaluating consistency of response, *Treximet* demonstrated consistent efficacy across multiple attacks.^(20,21,24) Individual patients also consistently responded to *Treximet* across attacks.

TREXIMET: EFFICACY IN PATIENTS WITH POOR RESPONSE TO SHORT-ACTING TRIPTANS

In two studies evaluating patients who reported poor response or intolerance to previous treatment with short-acting triptans, *Treximet* provided superior efficacy results versus placebo across a variety of endpoints.^(8,9,10)

TREXIMET: SAFETY

Treximet contains a boxed warning for cardiovascular and gastrointestinal risk. Please see complete product prescribing information for more information.

In clinical trials, *Treximet* was generally well-tolerated.^(16,17) ^(8,9,18,19) ^(20,21,22,23,10,24) The most common adverse events with *Treximet* are dizziness (4%), somnolence (3%), nausea (3%), chest discomfort/chest pain (3%), neck/throat, jaw pain/tightness/pressure (3%), paresthesia (2%), dyspepsia (2%), and dry mouth (2%).⁽²⁷⁾

Treximet has also been evaluated in a 12-month long-term safety trial.⁽²⁵⁾ The overall safety population included 565 patients who treated 24,485 attacks. The most common adverse events were nausea (6%), dyspepsia (2%), dizziness (3%), muscle tightness (3%), upper abdominal

pain (2%), paresthesia (2%), and chest discomfort (2%). One drug-related cardiovascular serious adverse event with *Treximet* was reported in the study.

Some information contained in this response may not be included in the approved Prescribing Information. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling.

In order for GlaxoSmithKline to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 888-825-5249. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

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